

CLINICAL REPORT

Widespread Livedoid Vasculopathy

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A 37-year-old woman with a 13-year history of widespread livedo reticularis and recurrent, painful ulcerative skin lesions was referred to our department because of a relapse of cutaneous manifestations of the skin lesions involving almost the whole body surface; malar erythema and oedema, non-scarring alopecia and fever were also associated. Routine laboratory data, immunological investigations and coagulation parameters were normal or negative. Histology was consistent with livedoid vasculopathy. A good clinical response was obtained using intravenous methylprednisolone combined with pentoxifylline. Livedoid vasculopathy is a rare, distinctive dermatosis that can be associated with systemic autoimmune disorders or present in an “idiopathic” form. The latter is at present regarded as a non-inflammatory thrombotic disease that may occur in patients with coagulation abnormalities. It is noteworthy that, in the present case, despite long-standing and dramatic cutaneous features, serious systemic complications have not developed and the patient’s seroimmunologic and coagulative profile has remained normal. Key words: autoimmune diseases; coagulation abnormalities; livedoid vasculopathy.

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Livedoid vasculopathy (LV) is a rare, distinctive dermatosis characterized by persistent livedo reticularis and recurrent painful ulcerative skin lesions, usually involving the lower extremities and resolving with hyperpigmentation and atrophic white scars (1). LV may be associated with infections or systemic autoimmune diseases (2), but sometimes no underlying disorder can be detected.

The latter, “idiopathic” form of LV is at present considered to be a non-inflammatory thrombotic disease due to occlusion of dermal small vessels (1, 3) that may occur in patients with coagulation abnormalities (4–7). We report a case of long-lasting and widespread LV in an adult female who showed a negative autoimmune profile and normal coagulation parameters.

CASE REPORT

A 37-year-old woman with a 13-year history of persistent livedo reticularis and recurrent, painful ulcerative skin lesions presented to our department after a one-month relapse of cutaneous features of the skin lesions. Simultaneously, a form of alopecia leading to almost total denudation of the scalp within a few days and malar erythema had developed. Livedo reticularis was initially confined to both lower extremities, gradually extending to involve almost the whole body surface. She had also suffered from recurrent painful skin ulcers of both lower limbs. Although some lesions had healed after many months, leaving white atrophic scars, new crops of active lesions appeared successively.

Except for a few months, the patient was never completely free of lesions. During her sole pregnancy a markedly aggravated tendency was seen. Her medical and surgical histories were unremarkable, without any report of arterial or venous thrombosis or spontaneous abortions or signs of Raynaud’s phenomenon. Repeated cycles of systemic corticosteroids in combination with a variety of topical agents had been tried by other dermatologists but with a poor clinical response.

Physical examination revealed widespread livedo reticularis in a “wide-mesh” net-like pattern and multiple, variously sized, well-demarcated ulcers over all four limbs, trunk and scalp, as well as a few eschars, surrounded by cyanotic skin, on the toes and soles (Figs 1 and 2). Non-scarring, total alopecia clinically consistent with alopecia areata (Fig. 3) and erythematous-violaceous oedema of the cheeks in a “butterfly-like” pattern were also found. On admission, the patient complained of fever (38.5°C), which impaired within a few days. Repeated blood cultures were negative. Routine laboratory investigations, including complete blood cell count, protein electrophoresis, liver and renal function tests, urinalysis were normal. Erythrocyte sedimentation rate (18 mm/1 h) and C-reactive protein (1.2 mg/dl), haemoglobin (11 g/dl) and haematocrit (31%) were close to the normal range. Autoimmune screening tests showed normal values, including IgG, IgA and IgM and complement C₃ and C₄ serum levels, anti-nuclear antibodies (ANA), as determined by indirect immunofluorescence (IIF) on Hep-2 cells, antibodies to extractable nuclear antigens (ENA), comprising SSA-Ro, SSB-La and Sm, as tested by enzyme-linked immunosorbent assay (ELISA), anti-double-stranded DNA



Fig. 1. Widespread livedo reticularis and multiple skin ulcers over all four limbs and trunk.

(dsDNA), as measured by Farr's method, anti-histone antibodies by immunoblotting, anti-thyroglobulin, anti-thyroid microsomal, anti-mitochondrial and anti-smooth muscle antibodies by IIF and rheumatoid factor. Normal tests were also obtained for the presence of lupus anticoagulant (LAC), detected using various coagulation tests, such as kaolin clotting time, silica clotting time and diluted Russel viper venom time, anticardiolipin antibodies (aCL) and anti-beta2-glycoprotein 1 (beta2-GP1) antibodies, measured by ELISA, antineutrophil cytoplasmic antibodies (ANCA), circulating immune complexes and cryoglobulins. A thyroid function test was within the normal range and serologies for hepatitis B and C, coxsackiae B, parvovirus and ECHO viruses were negative, while serologies for EBV and CMV were suggestive of previous infection. Also normal were the coagulation tests, including serum fibrinogen, fibrin and degradation products, thrombin time, activated partial thromboplastin time; the results for factor V Leiden and prothrombin 20210 mutation analysis were negative and factor VIII level was normal as were the functional levels of anti-thrombin III, protein C and protein S.



Fig. 2. Livedo and ulceronecrotic lesions surrounded by cyanotic skin on the toes and soles.

Radiography of the chest, sonographic examination of the abdomen and echocardiography as well as ophthalmologic investigation revealed no abnormalities.



Fig. 3. Non-scarring alopecia involving almost all scalp.

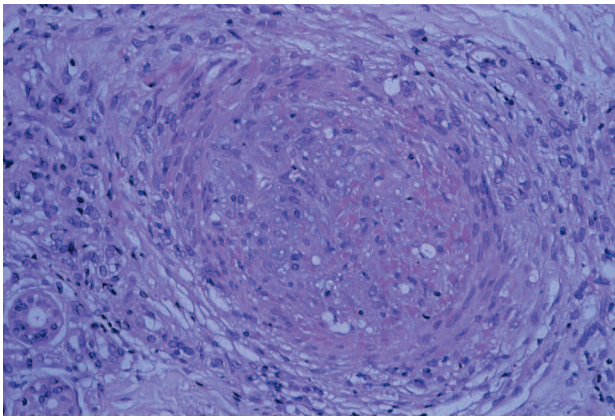


Fig. 4. Deep dermal ectatic blood vessel entirely occluded by microthrombi (haematoxylin and eosin stain; original magnification: $\times 400$).

Encephalic computed tomographic scan documented mild cerebral atrophy without focal parenchymal alterations.

A biopsy specimen from an ulcerative skin lesion showed superficial ulceration, a scant, mainly perivascular lymphohistiocytic infiltrate into the dermis and a deep dermal ectatic blood vessel entirely occluded by fibrinous microthrombus (Fig. 4). Direct immunofluorescence was negative. Based on the clinical and histopathologic features, a diagnosis of LV was made and the patient was given intravenous methylprednisolone 80 mg once daily for 5 days, followed by intramuscular and, subsequently, oral administration at progressively tapered dosage to 32 mg daily with pentoxifylline 400 mg twice daily associated for 2 months.

The treatment induced a marked clinical improvement over 2 weeks: the fever abated, cutaneous manifestations stopped developing and progressing and the intensity of livedo reticularis faded. Initial hair regrowth was also seen. Three months after the therapy, ulcerative skin lesions completely resolved, but the livedo reticularis persisted. With the aim of steroid sparing to 16 mg daily, Cyclosporin A was started at a dose of 200 mg daily for 3 months, while pentoxifylline was discontinued, resulting in further improvement of hair regrowth. After 6 months, she was in complete remission, apart from the livedo reticularis, on 8 mg of oral methylprednisolone daily.

DISCUSSION

LV is a rare cutaneous disease characterized clinically by persistent livedo reticularis and recurrent painful ulcerations that usually occur on the lower extremities (1). Histologically, LV usually shows segmental hyalinization, endothelial proliferation and thrombosis of the upper and mid-dermal small vessels associated with a mild, mainly perivascular, lymphocytic infiltrate.

In other cases, deeply situated dermal arterioles have shown obliterative changes. LV can occur in association with systemic autoimmune diseases, including systemic lupus erythematosus (SLE), systemic sclerosis and the so-called antiphospholipid syndrome (APS) (2); in these cases, immune-mediated mechanisms are considered to be responsible for vascular damage, leading to a true small vessel vasculitic process.

Our patient's cutaneous presentation, characterized by a widespread symmetric net-like pattern of livedo reticularis and multiple painful skin ulcers, was strongly suggestive of APS. However, international criteria for the diagnosis of APS, as recently revised (8), comprising vascular thrombosis and/or complications of pregnancy in association with LAC and/or aCL, were not fulfilled in our case.

Systemic hypercoagulopathies other than APS were also ruled out in the present case by performing a wide investigation of the coagulative function. The coexistence of malar rash in a "butterfly-like" pattern and fever was reminiscent of SLE, thus leading to the choice of a corticosteroid regimen; the good clinical response as well as the prompt resolution of fever following a pulse therapy with intravenous methylprednisolone were also consistent with autoimmune disease, but American Rheumatism Association criteria for diagnosis of SLE were lacking.

Livedo reticularis and skin ulcers can also occur in patients with subacute cutaneous lupus erythematosus (SCLE) (9), which represents a distinct subset of lupus erythematosus with unique clinical, serologic and immunologic features (10). However, the characteristic erythematous, non-scarring, papulosquamous and/or annular/polycyclic eruption as well as the serum markers of SCLE, namely Ro (SS-A) and La (SS-B) antibodies, were lacking in our patient.

Thus, on the basis of the clinical and histopathologic features, a diagnosis of LV could likely be made in our patient. The good clinical response to immunosuppressive therapy seems to suggest that immune-mediated pathomechanisms may play a cooperating role.

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